APPENDIX A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Tapas Mukhopadhyay, *et al.*	Group Art Unit: 1642
Serial No.: 10/043,877	Examiner: B. J. Fetterolf
Filed: January 9, 2002	Atty. Dkt. No.: INRP:095US
For: ANTIHELMINTHIC DRUGS AS A TREATMENT FOR HYPERPROLIFERATIVE DISEASES	

THIRD DECLARATION OF TAPAS MUKHOPADHYAY, SUNIL CHADA, ABNER MHASHILKAR, AND JACK A. ROTH UNDER 37 C.F.R. §1.131

We, Tapas Mukhopadhyay, Sunil Chada, Abner Mhashilkar, and Jack A. Roth, hereby declare as follows:

1. We are the joint inventors of the subject matter claimed in the above-referenced patent application, U.S.S.N. 10/043,887, filed January 9, 2002.

2. We previously submitted a declaration to set forth facts demonstrating that we both conceived the idea of the invention as reflected in the claims of the above-referenced patent application and determined that it functioned, prior to March 9, 1999.

3. In the present declaration we are submitting facts demonstrating that we steadily progressed in our research to confirm that our invention functioned in an animal model, which was in accordance with our initial understanding. We continually and

diligently conducted these studies from the time we conceived of our invention until the time our U.S. Provisional patent application, U.S.S.N. 60/261,346, was filed on January 11, 2001. Evidence of our diligence is set forth in Exhibits 1-3, discussed in detail below.

4. Submitted as Exhibit 1 to this declaration is a copy of a draft manuscript of our experiments and results, entitled "Potent Induction of Apoptosis by Anthelmintics in Human Lung Cancer Cells: Involvement of Wild-Type p53 and p21 Kinase Inhibitor." The studies set forth in this manuscript and the preparation of this manuscript took place prior to January 14, 2000.

5. Submitted as Exhibit 2 to this declaration is a copy a series of experiments and results involving the use of benzimidazoles in the treatment of p53 wild type expressing tumor cells, ending with animal models, as evidenced by the laboratory notebook of Dr. Jiichiro Sasaki, who worked under the direction of Dr. Tapas Mukhopadhyay. These experiments took place between November 10, 2000 and September 9, 2001.

6. Submitted as Exhibit 3 to this declaration is a copy of a draft manuscript of our experiments and results, including in animal models, entitled "Mebendazole: A Novel Microtubule Agent Having Potent Antitumor Activity," which was submitted for publication on October 25, 2001.

7. Exhibit 2 shows the preparation and results of a series of experiments pertaining to the benzimidazole drug, mebendazole (labeled MZ) for the treatment of cancer. Experiments pertaining to the treatment of cancer cells with mebendazole are listed on the following dates: November 11, 2000; November 15, 2000; December 5, 2000; December 8, 2000; December 12, 2000; January 11, 2001; January 12, 2001; January 18, 2001; February 10, 2001; February 20, 2001; February 23, 2001; February 26, 2001; March 2-6, 2001; March 19, 2001; March 20, 2001; March 29-31, 2001; April 3-4, 2001, April 14, 2001; April 19, 2001; April 26, 2001; June 6, 2001, June 7, 2001; June 16, 2001; July 24, 2001; July 26-28, 2001; August 1, 2001; August 4, 2001; August 5, 2001; August 7, 2001; August 31, 2001; August 31, 2001 and September 9, 2001. Of note, the last two entries pertain to the use of mebendazole in animal models.

8. Exhibit 3 shows the draft manuscript pertaining to the treatment of cancer cells with mebendazole on the inhibition of human tumor xenografts in mice. See Exhibit 3, Abstract, page 2. In accordance with our in vitro data, our animal model data showed that Mebendazole inhibited lung cancer growth. For example oral administration of mebendazole to mice previously injected with A549 lung cancer cells resulted in an 80% reduction in tumor count as compared to the control. See Exhibit 3, Results, page 10-11.

9. All work disclosed in the invention disclosure form was conducted in the United States of America.

10. Therefore, the invention as reflected in claims 75-77, 83-106, 161-162 and 184 of the above-referenced patent application was conceived of prior to March 9, 1999 and diligently reduced to practice.

11. We hereby declare that all statements made by our own knowledge are true and all statements made on information and belief are believed to be true and further that statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment under § 100 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issued thereon.

4/25/2006	Tapas Mukhopadhyay
Date	Tapas Mukhopadhyay
Date	Sunil Chada
Date	Abner Mhashilkar
Date	Jack A. Roth

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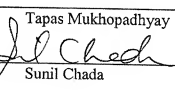
04/20/06 Date	 Sunil Chada
Date	Abner Mhashilkar
Date	Jack A. Roth

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Date	Sunil Chada
4/18/06 Date	Abhay Mhashilkar
Date	Jack A. Roth

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